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REMARKS

Claims 1-24, 28-31, 34, and 74-79 are pending in the subject application. Claims 11-16, 18, 24, 28-31, and 34 are withdrawn. Claims 25-27, 32, 33 and 35-73 were previously canceled without prejudice or disclaimer. By this Amendment, applicants have canceled claims 2-4 without disclaimer or prejudice, and have amended claims 1, 9, 17, 18, 20, 21, 28, 29, 34, 78, and 79. Support for the amendments to claims 1, 28, 29, 34, and 78 may be found, *inter alia*, in the specification at page 15, lines 28-32; page 31, lines 15-22. Applicants have amended claim 9 to delete reference to "PLG" and have amended claims 17, 18, 20, 21 to correct claim dependencies. Accordingly, these amendments do not raise any issue of new matter. Upon entry of this Amendment, claims 1, 5-10, 17, 19-23, and 74-79, as amended, will be pending and under examination.

Objection to the Specification:

The Examiner indicated that applicant is required to update the status of all parent priority applications in the first line of the specification.

In response, applicants note that the subject specification is §371 national stage of PCT/US02/28331, filed September 6, 2002 which claims the benefit of U.S. Provisional Application No. 60/370,410. Accordingly, applicants maintain that there is no change to the status of these applications and therefore no amendment to the priority paragraph in the subject application is required. Applicants maintain that the Examiner's objection does not apply to the subject application and respectfully request that the examiner reconsider and withdraw this ground of objection or clarify the basis for the objection.

Objection to the claims:

The Examiner objected to claim 9 because it refers to the chemical compound poly(lactic-co-glycolic acid) by its acronym PLG without first

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identifying it by its full name.

In response, applicants have hereinabove amended claim 9 to delete "(PLG)". Accordingly, applicants maintain that the Examiner's objection has been rendered moot and respectfully request that the Examiner reconsider and withdraw this claim objection.

The Invention

Applicants' invention provides a composition comprising (a) (i) a stable HIV-1 pre-fusion envelope glycoprotein trimeric complex operably affixed to (ii) an agent which is operably affixed to (iii) a pharmaceutically acceptable particle, (b) a pharmaceutically acceptable carrier, and (c) an adjuvant. The HIV-1 pre-fusion envelope trimeric complex comprises three monomeric units comprising a modified HIV-1 gp120 and a modified HIV-1 gp41 ectodomain, wherein the modified gp120 and the modified gp41 ectodomain are bound to each other by at least one intermolecular disulfide bond between a cysteine residue introduced into the modified gp120 and a cysteine residue introduced into the modified gp41 ectodomain. Applicants' claimed composition is useful as a therapeutic composition for inhibiting HIV-1 infection.

Double Patenting Rejections:

A. Over Claims of U.S. Serial No. 10/489,040 in view of O'Hagan et al.
The Examiner provisionally rejected claims 1-4, 6-10, 20, and 75-77 on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 113, 115-118, 120, and 124-126 of copending Application Serial No. 10/489,040 in view of O'Hagan et al. (2001).

As an initial matter, applicants note that the subject application is not commonly owned with Serial No. 10/489,040 which has a second owner in addition to the sole assignee of the subject application. Therefore, a nonstatutory obviousness-type double patenting rejection is not applicable. Moreover, Serial No. 10/489,040 per se is not a

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prior art reference as against the subject application.

Notwithstanding the foregoing, applicants note that currently pending claim 112 of U.S. Serial No. 10/489,040 recites a protein comprising a modified gp120 of a HIV-1 isolate, which includes a first cysteine introduced by a mutation, and a modified gp41 ectodomain of such HIV-1 isolate, which modified gp41 ectodomain includes a second cysteine introduced by a mutation, wherein (i) the modified gp41 polypeptide further comprises at least one mutation in its N-terminal helix, selected from the group consisting of V583, V580, L576, I573, T569, L566, Q562, Q590, L587, L555, Q552, I548, L545 and I559. Claims 113-116 recite specific clades and strains of HIV-1 isolates. Claim 117 and 118 recite specific cysteine substitutions in the modified gp120 and gp41. Claim 120 recites that the modified gp120 is further characterized by the absence or presence of one or more canonical glycosylation sites. Claims 124 recite a trimeric complex comprising three proteins as recited in claim 1 and claim 125 recites a composition comprising such trimeric complex. Claim 126 was canceled in Amendment submitted on November 20, 2006.

O'Hagan et al. describe various adjuvants suitable for use in vaccines against certain infectious diseases.

Applicants point out that none of the claims of U.S. Serial No. 10/489,040 recite a molecule which involves an HIV-1 trimeric complex operably affixed to an agent which is operably affixed to a pharmaceutically acceptable particle. O'Hagan et al. does not cure this deficiency as it only discloses adjuvants. Further, O'Hagan et al. do not disclose any agent linking any pharmaceutically acceptable particle to any antigen. Applicants also note that it would not have been obvious for one skilled in the art to delete the mutation in the N-terminal helix of the gp41 as recited in claim 112 of Serial No. 10/489,040.

Accordingly, applicants maintain that U.S. Serial No. 10/489,040 in combination with O'Hagan et al. would not render obvious applicants'

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claimed invention, even if it were properly citable which it is not. Applicants respectfully request that the Examiner reconsider and withdraw this provisional rejection on the grounds of obviousness-type double patenting.

B. Over Claims of U.S. Patent No. 7,022,324 in view of O'Hagan et al.
The Examiner rejected claims 3-6, 8-10, 20, and 74-79 on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-15 and 18-20 of Binley et al., U.S. Patent No. 7,022,324 ("Binley et al.") in view of O'Hagan et al. (2001).

Once again, applicants note as an initial matter that U.S. Patent No. 7,022,324 and the subject application are not commonly owned. The subject application has a sole assignee whereas U.S. Patent 7,022,324 has two assignees one of which is the assignee of this application. Therefore, a nonstatutory obviousness-type double patenting rejection is not applicable.

Notwithstanding the foregoing, applicants note that claim 1 of Binley et al. recites a complex of a modified gp120 comprising an A492C mutation and a modified gp41 ectodomain comprising a T596C mutation, wherein the modified gp120 and the modified gp41 ectodomain are joined together by an intermolecular disulfide bond. Claims 2-7 further characterize the complex of claim 1. Claim 8 recites a trimer which comprises three identical complexes as recited in claims 1-7. Claim 9 recites a modified gp140 polypeptide of a HIV-1 isolate comprising two portions, the first portion corresponding to the modified gp120 as recited in claim 1 and the second portion corresponding to the modified gp41 ectodomain as recited in claim 1. Claims 10-17 further characterize the modified gp140 polypeptide of claim 9. Claim 18 recites a trimer comprising three identical modified gp140 polypeptides as recited in claims 9-17. Claim 19 recites a composition comprising a carrier and either the complex as recited in claims 1-7 or the trimer as recited in claims 8 or 18. Claim 19 recites the composition of claim 18 further comprising an adjuvant.

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As stated above, O'Hagan et al. describe various adjuvants suitable for use in vaccines against certain infectious diseases.

Applicants point out that none of the claims of Binley et al. recite a molecule which involves a HIV-1 trimeric complexes operably affixed to an agent which is operably affixed to a pharmaceutically acceptable particle.

Neither Binley et al. nor O'Hagan et al. discloses an agent linking a trimeric complex to a pharmaceutically acceptable particle.

Accordingly, applicants maintain that Binley et al. in combination with O'Hagan et al. would not render obvious applicants' claimed invention, even if it were properly cited which it is not. Applicants respectfully request that the Examiner reconsider and withdraw this provisional rejection on the ground of obviousness-type double patenting.

Rejections Under 35 U.S.C. §103(a)

A. Barnett et al. in view of Binley et al.:

The Examiner rejected claims 1, 3-10, 20-23, and 74-79 under 35 U.S.C. §103(a) as allegedly unpatentable over Barnett et al. (U.S. Patent No. 6,602,705 B1) in view of Binley et al. (U.S. Patent No. 7,022,324). Specifically, the Examiner stated that Barnett et al. describe antigen-presenting and immune-stimulating compositions that include various excipients, adjuvants, carriers, and modulating agents. The Examiner also stated that Barnett et al. does not disclose an intermolecular disulfide bond between cysteine residues introduced by mutations A492C and T596C. The Examiner further stated that Binley et al. disclose an isolated HIV-1_{JRFL} envelope glycoprotein complex comprising a gp120 and gp41 bound to one another by a disulfide bond between a cysteine residue introduced by an A492C mutation into gp120 and a cysteine residue introduced by a T596C mutation into gp41, wherein the gp41 further comprises a mutated furin cleavage site and is characterized by the presence of one or more canonical glycosylation site not present in

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wildtype gp120 or by the absence of one or more glycosylation sites present in wildtype gp120.

In response, applicants respectfully traverse the Examiner's ground of rejection and maintain that applicants' claimed invention is not obvious.

Barnett et al. disclose modified gp140 and gp120 polypeptides and the assembly of such expressed polypeptides into virus-like particles (VLPs).

As stated above, Binley et al. disclose monomeric complexes or modified gp140 polypeptides which involve a modified gp120 having an A492C mutation and a modified gp41 ectodomain having a T596C mutation, wherein the modified gp120 and the modified gp41 ectodomain are joined together by an intermolecular disulfide bond. Binley et al. also discloses trimers of such monomers.

Applicants maintain that neither Barnett et al. nor Binley et al. disclose a molecule in which a HIV-1 trimeric complex is operably affixed to an intermediary agent which is operably affixed to a pharmaceutically acceptable particle, as recited in claim 1 as amended.

Applicants maintain that Barnett et al. do not teach any intermediary agent. The HIV virus like particles disclosed in Barnett et al. are not bound, i.e. operably affixed, to any other molecule. Applicants further maintain that Binley et al. does not disclose trimers operably affixed to a pharmaceutically acceptable particle, and certainly not via an agent such as recited in applicants' claims.

Accordingly, applicants maintain that the combination of Barnett et al. and Binley et al. do not render obvious applicants' claimed invention because a combination would not include each and every element of applicants' claimed composition. It is thus respectfully requested that the Examiner reconsider and withdraw this ground of rejection.

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B. Barnett et al. in view of Binley et al. and Ishikawa et al.:

The Examiner further rejected claims 2, 17, and 19 under 35 U.S.C. §103(a) as allegedly unpatentable over Barnett et al. (U.S. Patent No. 6,602,705 B1) in view of Binley et al. (U.S. Patent No. 7,022,324), and in further view of Ishikawa et al. (1998). Specifically, the Examiner stated that Ishikawa et al. describe that antibody IgGs to HIV-1 were reacted with polystyrene beads coated successively with affinity purified (anti-2,4-dinitrophenyl group) IgG and HIV-1 antigen conjugates and subsequently with HIV-1 antigen β -D-galactosidase conjugates. The Examiner further stated that it would have been obvious for one skilled in the art to modify the immune complexes of Ishikawa et al. by modifying the composition of Binley et al. by affixing the HIV-1 gp120-gp41 trimer to a particle via an IgG as taught by Ishikawa et al.

In response, applicants respectfully traverse the Examiner's ground of rejection.

Applicants again maintain that neither Barnett et al. nor Binley et al. disclose a molecule in which a pharmaceutically acceptable particle is operably linked to an intermediary agent which is operably linked to HIV-1 trimeric complexes as recited in amended claim 1.

Ishikawa et al. disclose an immunoassay using immune complexes affixed to a polystyrene bead. More particularly, Ishikawa et al. disclose and teach improved solid phase immunoassays for determining HIV-1 infection by detecting HIV-1 p24 antigen and antibodies to HIV-1 p17, reverse transcriptase, and gp41 antigens in a test sample. The immunoassays of Ishikawa et al. can detect various HIV-1 antigens and anti-HIV-1 antibodies at an early time after infection when these components may be at low levels in serum. The immunoassays of Ishikawa et al. are sequential immune complex transfer enzyme immunoassays that employ conjugates of different components, which are affixed to polystyrene beads to capture HIV-1 antigens and anti-HIV-1 antibodies (IgGs) in a patient's sample, e.g., serum.

For example, to detect antibodies directed against an HIV-1 antigen,

such as HIV-1 p17, the sequential immunoassay described by Ishikawa et al. involves the formation of a complex between an anti-p17 antibody and a solid phase capture reagent formed by coating the solid phase with anti-DNP (2,4-dinitrophenyl group) IgG antibodies, which had been reacted with DNP-HIV-1 p17 antigen. The anti-HIV-1 p17 antibody was bound to the solid phase via the formation of a complex comprising the solid phase-bound anti-DNP antibody bound to the DNP-HIV-1 p17 antigen. This complex was next reacted with HIV-1-p17 antigen bound to β -galactosidase to form a larger complex comprising the anti-HIV-1 p17 antibody, the DNP-HIV-1 p17 conjugate and the HIV-1 p17- β -galactosidase conjugate, which was subsequently transferred to another solid phase coated with an anti-human IgG gamma-chain antibody (which reacts with the anti-HIV-1 p17 antibody bound to the DNP-p17 conjugate and to the p17- β -galactosidase conjugate. The sequential formation of the immune complexes in Ishikawa et al.'s immunoassay is depicted schematically in Fig. 2 ("Present (sequential) immunoassay"), page 233, of Ishikawa et al. As described by Ishikawa et al., the immune complexes comprising the three components on a solid phase was rapidly formed by coating a polystyrene bead successively with the anti-DNP antibody and the DNP-HIV-1 p17 antigen conjugate. The so-coated bead was incubated with serum containing anti-HIV-1 p17 antibodies and then with the HIV-1 p17- β -galactosidase conjugate at high concentrations. (See, Ishikawa et al. at page 233, second paragraph, column one and first paragraph, column two).

The sequential immunoassays of Ishikawa et al. are described as allowing a larger amount of complex comprising the three components in the assay to form more rapidly on the polystyrene bead compared with previous methods, thereby providing a higher amount of enzyme activity (or signal) when the immunoassay is performed.

Applicants maintain that the disclosure of Ishikawa regarding immunoassays does not render obvious applicants' claimed composition. Applicants maintain that one skilled in the art would not utilize the teachings of Ishikawa, i.e. an improved immunoassay, to make applicants'

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claimed composition which is formulated for its intended purpose, e.g. administration to a subject to inhibit HIV infection of cells, not for detection of a captured antigen on a solid support. Thus, Ishikawa et al. do not disclose the use of an adjuvant because an adjuvant would not be used in an immunoassay unlike applicants' now claimed composition which requires the presence of an adjuvant. Applicants maintain that the immunoassay teachings of Ishikawa et al. would not be employed to make a therapeutic composition as now claimed.

Accordingly, applicants maintain that the combination of Barnett et al. in view of Binley et al. and Ishikawa et al. does not render obvious applicants' invention as now claimed.

For the above reasons, applicants maintain that claim 1 as amended and claims dependent thereon are not obvious over the combination of Barnett et al. and Binley et al. or that of Barnett et al., Binley et al. and Ishikawa et al. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this ground of rejection.

Conclusion

In view of the amendments to the claims and the remarks made hereinabove, applicants respectfully submit that the grounds of objection and rejection set forth in the October 5, 2006 Office Action have been overcome. Applicants therefore respectfully request that the Examiner reconsider and withdraw these grounds of objection and rejection, and request allowance of all claims now under examination, i.e. claims 1, 5-10, 17, 19-23, and 74-79.

Further, applicants request that upon allowance of claims 1, 5-10, 17, 19-23, and 74-79, the Examiner rejoin and allow claims 11-16, 18, 24, 28-31, and 34 which depend on and incorporate all features of amended claim 1.

If a telephone interview would be of assistance in advancing prosecution of this application, applicants' undersigned attorney invites the Examiner to telephone him at the number provided below.

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SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, applicants direct the Examiner's attention to the following documents listed below, certain of which are also listed on Substitute Form PTO-1449 (**Exhibit A**).

This Supplemental Information Disclosure Statement is being submitted pursuant to 37 C.F.R. §1.97(c) before the mailing of a Final Office Action, Notice of Allowance or an action that otherwise closes prosecution of the application. Pursuant to 37 C.F.R. §1.97(c)(2), the fee set forth in §1.17(p) must accompany this Supplemental Information Disclosure Statement. The fee set forth in §1.17(p) is ONE HUNDRED AND EIGHTY DOLLARS (\$180.00) and a check including this amount is enclosed. Accordingly, applicants request that this Supplemental Information Disclosure Statement be entered and considered.

In accordance with 37 C.F.R. §1.92(a)(2)(ii), copies of U.S. Patents and U.S. Patent Application Publications listed herein need not be provided. Accordingly, copies of documents listed below as items 1-9 are not submitted herewith. Copies of documents listed below as items 10-74 are attached hereto as **Exhibits 1-66**.

1. U.S. Patent No. 5,935,579, issued August 10, 1999 to Habeshaw et al.;
2. U.S. Patent No. 5,474,914, issued December 12, 1995 to Spaete;
3. U.S. Patent No. 5,886,163, issued March 23, 1999 to Maddon et al.;
4. U.S. Patent No. 6,171,596, issued January 9, 2001 to Earl et al.;
5. U.S. Patent No. 6,710,173, issued March 23, 2004 to Binley et al.;

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6. U.S. Application Publication No. 2003-0052839, published March 20, 2003;
7. U.S. Patent Application Publication No. 2004/0191269, published 9/30/04;
8. U.S. Application Publication No. US 2005-0089526, published April 28, 2006;
9. U.S. Application Publication No. US 2004-0224308, published November 11, 2004;
10. U.S. Application Publication No. 2006-0094049, published May 4, 2006;
11. U.S. Serial No. 10/117,366, filed April 5, 2002, (**Exhibit 1**);
12. U.S. Serial No. 09/340,992, filed June 25, 1999 (**Exhibit 2**);
13. U.S. Provisional Application No. 60/141,168, filed June 25, 1999 (**Exhibit 3**);
14. U.S. Provisional Application No. 60/370,410, filed April 5, 2002 (**Exhibit 4**);
15. U.S. Provisional Application No. 60/317,775, filed September 6, 2001 (**Exhibit 5**);
16. U.S. Provisional Application No. 60/370,264, filed April 5, 2000 (**Exhibit 6**);
17. U.S. Provisional Application No. 60/317,910, filed September 6, 2001 (**Exhibit 7**);
18. U.S. Provisional Application No. 60/317,909, filed September 6, 2001 (**Exhibit 8**);

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19. U.S. Provisional Application No. 60/317,764, filed September 6, 2001 (**Exhibit 9**);
20. U.S. Provisional Application No. 60/580,229, filed March 5, 2004 (**Exhibit 10**);
21. International PCT Application Publication No. WO/2006/002079, published January 5, 2006 (**Exhibit 11**);
22. International PCT Application Publication No. WO 2003/087757, published October 23, 2003 (**Exhibit 12**);
23. International PCT Application Publication No. WO 2003/022869, published March 20, 2003 (**Exhibit 13**);
24. International PCT Application Publication No. WO 2001/00648 A1, published January 4, 2001 (**Exhibit 14**);
25. Atwell, et al. (1997) "Stable Heterodimers From Remodeling The Domain Interface Of A Homodimer Using A Phage Display Library" J. Mol. Biol. 270:26-35 (**Exhibit 15**);
26. Barouch, D.H. et al. (2002) "Eventual AIDS Vaccine Failure In The Rhesus Monkey By Viral Escape From Cytotoxic T Lymphocytes" Nature 415:335-339 (**Exhibit 16**);
27. Barouch, D.H. et al. (2000) "DNA Vaccination For HIV-1 And SIV" Intervirology. 4:282-287 (**Exhibit 17**);
28. Binley, J.M. et al. (2002) "Enhancing The Proteolytic Maturation Of Human Immunodeficiency Virus Type 1 Envelope Glycoproteins." J. of Virology, 76 (6): 2606-2616 (**Exhibit 18**);
29. Binley, J.M. et al. (2000) "A Recombinant Human Immunodeficiency Virus Type 1 Envelope Glycoprotein Complex Stabilized By An

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Intermolecular Disulfide Bond Between The gp120 And gp41 Subunits
Is An Antigenic Mimic Of The Trimeric Viron-Associated Structure"
J. Virol. 627-643 (**Exhibit 19**);

30. Burton, D.R. et al. (1994) "Efficient Neutralization Of Primary Isolates Of HIV-1 By A Recombinant Human Monoclonal Antibody" Science 266:1024-1027 (**Exhibit 20**);
31. Burton, D.R. et al. (1998) "Why Do We Not Have An HIV Vaccine And How Can We Make One? Nature Med. Vaccine Suppl. 4(5):495-498 (**Exhibit 21**);
32. Cao, J. et al. (1993) "Effects Of Amino Acid Changes In The Extracellular Domain Of The Human Immunodeficiency Virus Type 1 Gp41 Envelope Glycoprotein" J. Virol. 67(5):2747-2755 (**Exhibit 22**);
33. Cao, et al. (1997) "Replication And Neutralization Of Human Immunodeficiency Virus Type 1 Lacking The V1 And V2 Variable Loops Of The gp120 Envelope Glycoprotein" J. Virol. 71:9808-9812 (**Exhibit 23**);
34. Chen, S. (1993) "Mutational Analysis Of The Leucine Zipper-Like Motif Of The Human Immunodeficiency Virus Type 1 Envelope Transmembrane Glycoprotein." J. of Virology 67 (6):3615-3619 (**Exhibit 24**);
35. Ditzel H J et al. (1997) "Mapping The Protein Surface Of Human Immunodeficiency Virus Type 1 gp 120 Using Human Monoclonal Antibodies From Phage Display Libraries" J. of Molecular Biology, 267 (3):684-695 (**Exhibit 25**);
36. Edinger, et al. (1999) "Functional Dissection Of CCR5 Coreceptor Function Through The Use Of CD4-Independent Simian Immunodeficiency Virus Strains" J. Virol. 73:4062-4073 (**Exhibit**

26);

37. Farzan, M. et al. (1998) "Stabilization Of Human Immunodeficiency Virus Type 1 Envelope Glycoprotein Trimers By Disulfide Bonds Introduced Into The gp 41 Glycoprotein Ectodomain" J. Virol. 72:7620-7625 (**Exhibit 27**);
38. Fouts, et al. (1998) "Interactions Of Polyclonal And Monoclonal Anti-Glycoprotein 120 Antibodies With Oligomeric Glycoprotein 120-Glycoprotein 41 Complexes Of A Primary HIV Type 1 Isolate: Relationship To Neutralization" AIDS Res Human Retrovir. 14:591-597 (**Exhibit 28**);
39. Fouts, et al. (1997) "Neutralization Of The Human Immunodeficiency Virus Type 1 Primary Isolate JR-FL By Human Monoclonal Antibodies Correlates With Antibody Binding To The Oligomeric Form Of The Envelope Glycoprotein Complex" J. Virol. 71:2779-2785 (**Exhibit 29**);
40. Gallaher, et al. (1995) "A General Model For The Surface Glycoproteins Of HIV And Other Retroviruses" AIDS Res. Human Retrovir. 11:191-202 (**Exhibit 30**);
41. Johnston, M.I. et al. (2001) "Progress In HIV Vaccine Development" Curr. Op. Pharmacol. 1(5):504-510 (**Exhibit 31**);
42. Joy, A.K. et al. (1999) "Can HIV Infection Be Prevented With A Vaccine? Drugs R&D 6:431-440 (**Exhibit 32**);
43. Haynes, B.F. (1996) "Update On The Issues Of HIV Vaccine Development" Ann. Med. 28:39-41 (**Exhibit 33**);
44. Haynes, B.F. (1996) "HIV Vaccines: Where Are We And We Are We Going?" Lancet 348:933-937 (**Exhibit 34**);

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45. Helseth, E. et al. (1991) "Human Immunodeficiency Virus Type 1 gp120 Envelope Glycoprotein Regions Important For Association With The gp41 Transmembrane Glycoprotein" J. Virol. 65(4):2119-2123 (**Exhibit 35**);
46. Labranche, C. et al. (1994) "ERRATUM Biological, Molecular, And Structural Analysis Of A Cytopathic Variant From A Molecularly Cloned Simian Immunodeficiency Virus" J. Virol. 68:7665-7667 (**Exhibit 36**);
47. Labranche, C. et al. (1994) "Biological, Molecular, And Structural Analysis Of A Cytopathic Variant From A Molecularly Cloned Simian Immunodeficiency Virus" J. Virol. 68:5509-5522 (**Exhibit 37**);
48. Letvin, N.L. (1998) "Progress In The Development Of An HIV-1 Vaccine" Science 280:1875-1880 (**Exhibit 38**);
49. Maerz, A.L. et al. (2001) "Functional Analysis Of The Disulfide-Bonded Loop/Chain Reversal Region Of Human Immunodeficiency Virus Type 1 gp41 Reveals A Critical Role In gp120-gp41 Association" J. Virol. 75(14):6635-6644 (**Exhibit 39**);
50. McInerney, T. et al. (1998) "Mutation-Directed Chemical Cross-Linking Of Human Immunodeficiency Virus Type 1 gp41 Oligomers" J. Virol. 72:1523-1533 (**Exhibit 40**);
51. Mitchell, et al. (1998) "Inactivation Of A Common Epitope Responsible For The Induction Of Antibody-Dependent Enhancement Of HIV" AIDS 12:147-156 (**Exhibit 41**);
52. Moore, et al. (1994) "Probing The Structure Of The Human Immunodeficiency Virus Surface Glycoprotein Gp120 With A Panel Of Monoclonal Antibodies" J. Virol. 68:469-484 (**Exhibit 42**);
53. Moore, et al. (1994b) "Immunological Evidence For Interactions

- Between The First, Second, And Fifth Conserved Domains To The Gp120 Surface Glycoprotein Of Human Immunodeficiency Virus Type 1" J. Virol. 68(11):6836-6847 (**Exhibit 43**);
54. Murphy, F.A. (1996) in Fields Virology, 3rd Edition, Fields, B.N. et al. eds., Lippincott-Raven Publishers, Philadelphia, 40-41 (**Exhibit 44**);
56. Nakashe, J. et al., (2001) "Rectal Immunization With Antigen-Containing Microspheres Induces Stronger Th2 Responses Than Oral Immunization: A New Method For Vaccination" Vaccine, Butterworth Scientific Guildford, GB, 20 (3-4):377-384 (**Exhibit 45**);
57. Parker, Carole, et al. (2001) "Fine Definition Of The Epitope On The Gp41 Glycoprotein Of Human Immunodeficiency Virus Type 1 For The Neutralizing Monoclonal Antibody 2F5" J. of Virol. 75 (22):10906-10911 (**Exhibit 46**);
58. Parren, et al. (1997) "HIV-1 Antibody - Debris Or Virion?" Nat. Med. 3:366-367 (**Exhibit 47**);
59. Parren, et al. (1998) "Neutralization Of Human Immunodeficiency Virus Type 1 By Antibody To gp120 Is Determined Primarily By Occupancy Of Sites On The Virion Irrespective Of Epitope Specificity" J. Virol. 72:3512-3519(**Exhibit 48**);
60. Reitter, et al. (1998) "A Role For Carbohydrates In Immune Evasion In AIDS" Nat. Med. 4:679-684 (**Exhibit 49**);
61. Sanders R. et al., (2002) "Stabilization Of The Soluble, Cleaved, Trimeric Form Of The Envelope Glycoprotein Complex Of Human Immunodeficiency Virus Type 1" Journal of Virology, 76 (17):8875-8889 (**Exhibit 50**);
62. Schulke et al. (2002) "Oligomeric And Conformational Properties Of A Proteolytically Mature, Disulfide-Stabilized Human

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Immunodeficiency Virus Type 1 gp140 Envelope Glycoprotein" J. of Virology, 76 (15):7760-7776 (**Exhibit 51**);

63. Schulz, et al. (1992) "Conserved Structural Features In The Interaction Between Retroviral Surface And Transmembrane Glycoproteins?" AIDS Res. Hum. Retrovirus 8(9):1571-1580 (**Exhibit 52**);
64. Stamatatos, L. et al. (1994) "Differential Regulation Of Cellular Tropism And Sensitivity To Soluble CD4 Neutralization By The Envelope gp120 Of Human Immunodeficiency Virus Type 1" J. Virol. 68:4973-4979 (**Exhibit 53**);
65. Trkola A. et al. (1996) "Human Monoclonal Antibody 2g12 Defines A Distinctive Neutralization Epitope On The gp120 Glycoprotein Of Human Immunodeficiency Virus Type 1" J. Virol. 70:1100-1108 (**Exhibit 54**);
66. April 15, 2004 International Search Report for International PCT Application No. PCT/US02/28331, filed September 6, 2002 (**Exhibit 55**);
67. May 12, 2004 International Search Report for International PCT Application No. PCT/US02/28332, filed September 6, 2002 (**Exhibit 56**);
68. September 7, 2000 International Search Report for Application No. PCT/US00/17267, filed June 23, 2000 (**Exhibit 57**);
69. January 23, 2002 International Preliminary Examination Report for Application No. PCT/US00/17267, filed June 23, 2000 (**Exhibit 58**);
70. March 5, 2003 Supplementary European Search Report for Application No. EP 00 94 4801 (**Exhibit 59**);

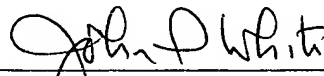
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71. June 11, 2003 Supplementary European Search Report for App. No. EP00944801 (**Exhibit 60**);
72. August 22, 2006 Supplementary European Search Report for Application No. EP/02770472 3 (**Exhibit 61**);
73. August 31, 2006 Supplementary European Search Report for Application No. EP/0277047 (**Exhibit 62**);
74. Josephson, et al. (1999) "High-Efficiency Intracellular Magnetic Labeling With Novel Superparamagnetic-Tat Peptide Conjugates" *Bioconjugate Chemistry*, Vol. 10 pages 186-191 (**Exhibit 63**);
75. Rickman et al. (1991) "Use of Adjuvant Containing Mycobacterial Cell Wall Skeleton, Monophosphoryl Lipid A, And Aqualene In Malaria Circumsporozoite Protein Vaccine" *The Lancet*, Vol. 337, pgs 998-1001 (**Exhibit 64**);
76. December 27, 2006 International Search Report for PCT/US05/21091, filed June 15, 2005 (**Exhibit 65**); and
77. February 1, 2007 International Preliminary Report for PCT/US05/21091, filed June 15, 2005 (**Exhibit 66**).

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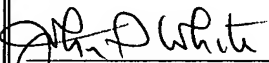
No fee, other than the enclosed \$510.00 fee for a three-month extension of time and the enclosed \$180.00 fee for filing a Supplemental Information Disclosure Statement, is deemed necessary in connection with the filing of this Amendment. However, if any additional fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 03-3125.

Respectfully submitted,



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